

# AKI in ICU

## An Overview

By

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# Epidemiology

- Up to 18% of hospitalized patients with baseline normal renal function experience AKI
- Up to 4% of hospital admissions are due to AKI
- Mortality may reach up to 70% in AKI requiring RRT

## Kidney Disease: Improving Global Outcomes (KDIGO) Composite Staging of AKI

Stage	Serum Creatinine	Urine Output
1	1.5-1.9x baseline OR ≥0.3 mg/dl (≥26 μmol/l) increase	<0.5 ml/kg/h for 6-12 h
2	2.0-2.9x baseline	<0.5 ml/kg/h for ≥12 h
3	3.0x baseline OR Increase in serum creatinine to ≥4.0 mg/dl (≥352 μmol/l) OR Initiation of renal replacement therapy OR, in patients younger than 18 years, decrease in eGFR to <35 ml/min/1.73 m <sup>2</sup>	<0.3 ml/kg/h for ≥24 h OR Anuria for ≥12 h

TABLE 2: Summary of original reports describing the incidence of AKI.

Author	no. of subjects	Single/multicenter	Patient population	AKI definition used	AKI incidence (%)	Mortality endpoint	Mortality (%)
Thakar et al. [3]	325,395	Multi	Mixed	RIFLE	22	ICU	10.9
Ostermann and Chang [4]	41,972	Multi	Mixed	RIFLE	35.8	ICU Hospital	10.2 12.9
Gammelager et al. [5]	30,762	Multi	Mixed	RIFLE	15.6	30 days	40
Joannidis et al. [6]	16,784	Multi	Mixed	RIFLE	35.5	Hospital	36.4
Mandelbaum et al. [7]	14,524	Single	Mixed	AKIN	57	ICU Hospital	7.1 9.1
Hoste et al. [8]	5383	Single	Mixed	RIFLE	67.2	Hospital	13.3
Cruz et al. [9]	2164	Multi	Mixed	RIFLE	10.8	ICU	36.3
Samimagham et al. [10]	1026	Single	Mixed	RIFLE	21.7	1 year	49 2.5 RRT at 90 d
Fonseca Ruiz et al. [11]	794	Single	Mixed	AKIN	39.8	ICU Hospital	25.4 32.1
Piccinni et al. [12]	576	Multi	Mixed	RIFLE	42.7	ICU	29
Medve and Gondos [13]	459	Single	Mixed	AKIN	24.4	ICU Hospital	39.3 49.1
Samimagham et al. [10]	235	Single	Mixed	AKIN	31.1	ICU	72.6
Yue et al. [14]	191	Single	Mixed	AKIN	35.5	ICU	48
Abosaif et al. [15]	183	Single	Mixed	RIFLE		ICU	47.5

# Why kidney is easily exposed to Toxin and Drug

- Blood flow  $1/3$  of cardiac output
- High energy demand
- Water reabsorption, increase concentration of toxic materials
- Tubular reabsorption and secretion of some drugs



## Specific Risk Factors for the Development of Acute Kidney Injury (AKI) in Common Clinical Situations

### Postoperative (General)

#### Miscellaneous

Age <70 yr  
Proteinuria  
Hyperglycemia  
Hypertension  
Massive blood transfusion

#### Hemodynamic

Congestive heart failure  
Aortic cross-clamping  
Cardiac instability  
Major vascular surgery  
Infection/sepsis  
Multiorgan failure

#### Gastrointestinal and Endocrine

Cirrhosis/biliary surgery  
Obstructive jaundice  
Diabetes mellitus

### Cardiac Surgery

Female gender  
COPD  
Proteinuria  
Preoperative  $S_{cr} > 2.1$  mg/dl  
Anemia  
Insulin-requiring diabetes

ACE inhibitor therapy  
Heart failure  
LV ejection fraction <35%  
Preoperative IABP  
Hyperglycemia

Emergency surgery  
Valve surgery only  
Previous cardiac surgery  
Other cardiac surgery  
Combination of CABG + valve surgery  
Blood transfusion

### Critically Ill

High A-a gradient\*  
Low serum albumin  
Proteinuria  
Hyperglycemia  
High intraabdominal pressure  
Active cancer

### Sepsis

Age  
 $S_{cr} > 1.3$  mg/dl  
Serum bilirubin >1.5 mg/dl  
Elevated CVP >8 cm  
Hemodynamic instability

# Risk Factors contd.,

## Contrast Nephropathy

Age >75 yr	Volume of contrast >100 ml
Heart failure	Intra-arterial injection
Diabetes mellitus	Systolic BP <80 mm Hg for >1 hr and need for inotropic support or IABP 24 hr after procedure
$S_{Cr} > 1.5$ mg/dl or eGFR <60 ml/min/1.73 m <sup>2</sup>	Use of IABP

History of pulmonary edema

Anemia/blood loss (Hct: <39% for men; <36% for women)

Nephrotoxic antibiotics

**Aminoglycosides**

**Amphotericin**

Old age

Volume depletion

Pre-existing renal dysfunction

Concurrent other nephropathy

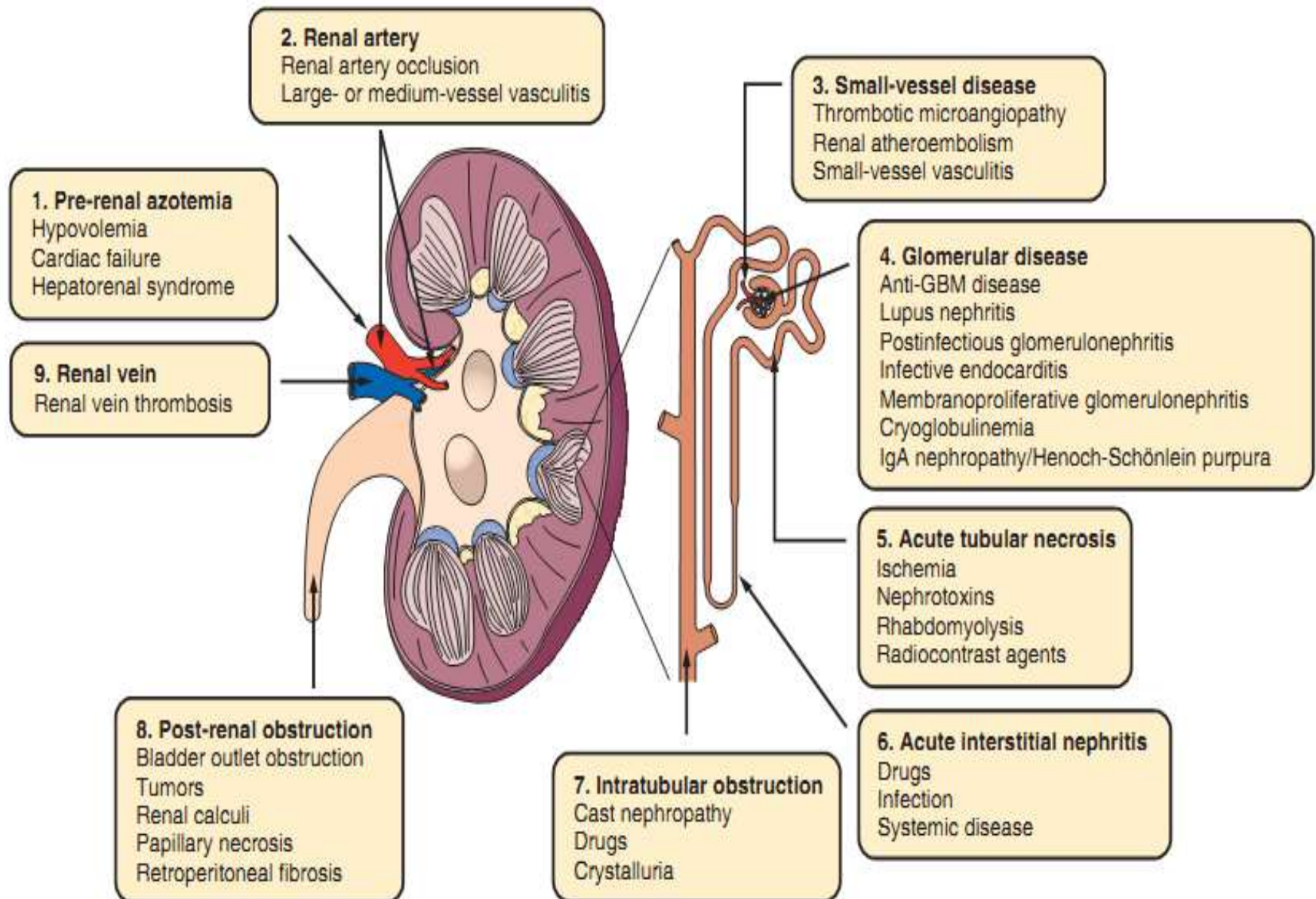
Duration of therapy >7 days

Volume depletion

Divided dose regimens

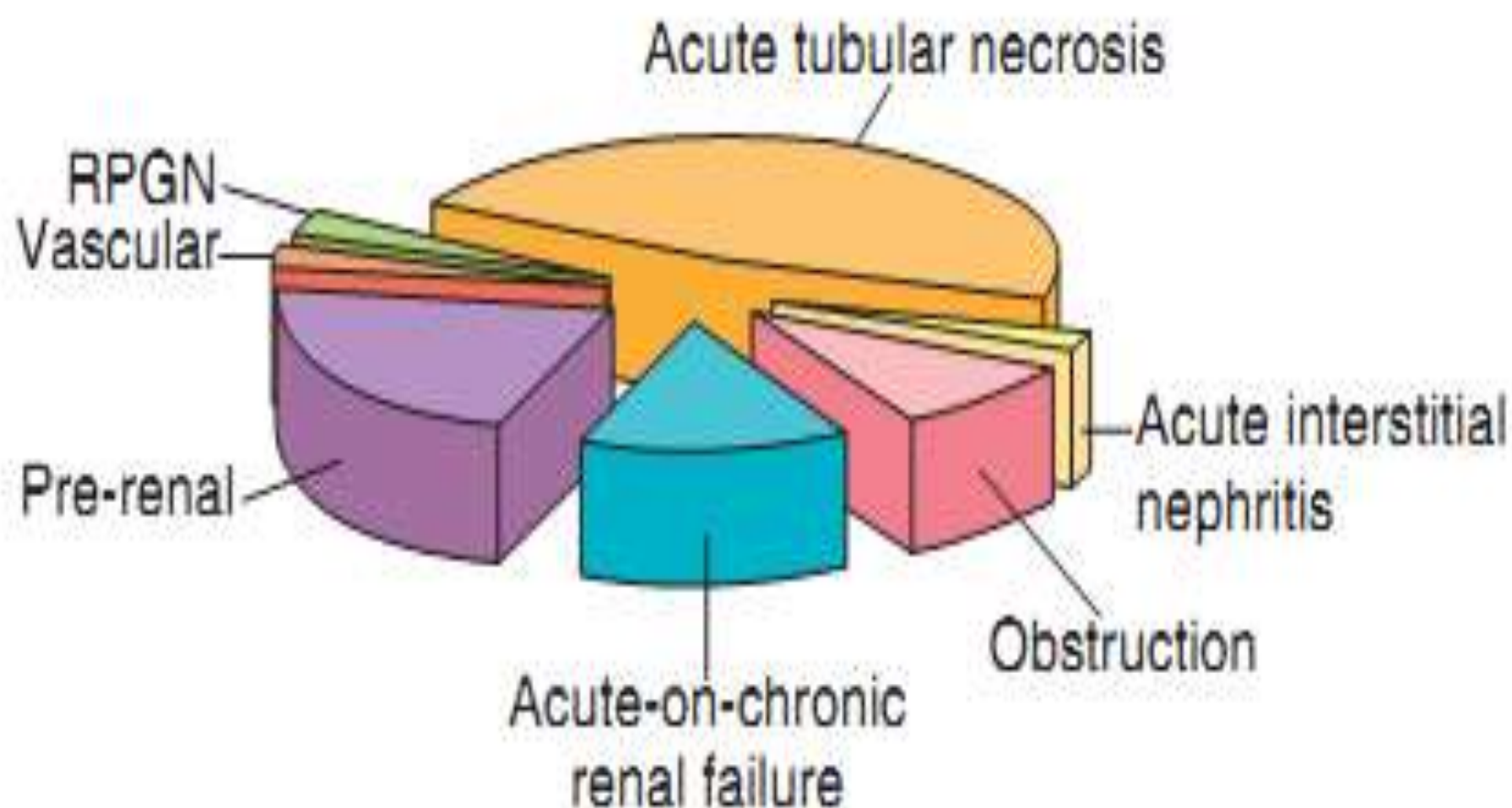
Liver disease

# Causes of AKI

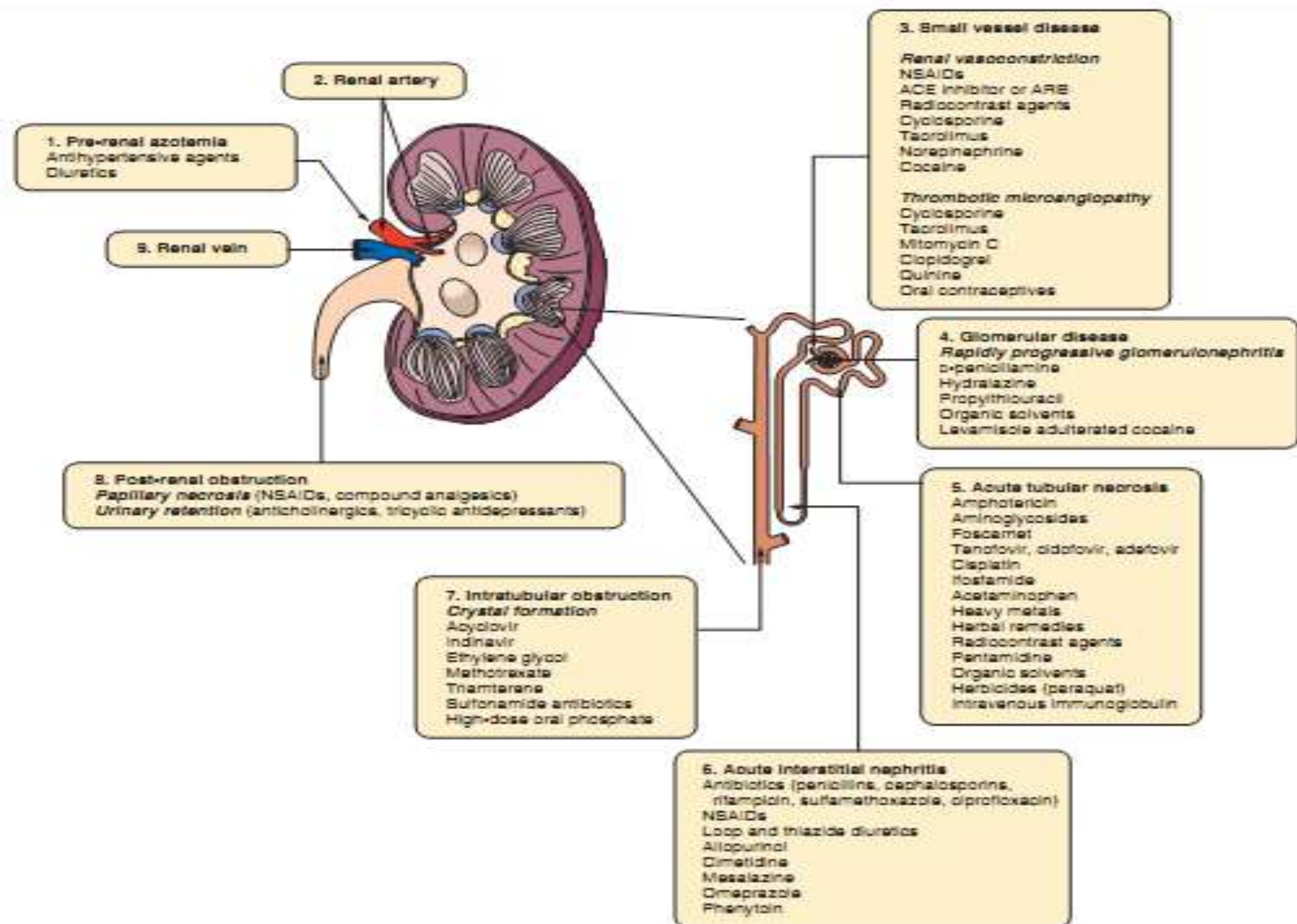




# Causes of AKI in Hospital Setting



## Nephrotoxic Agents Leading to Acute Kidney Injury



# Contd.,

## Causes of Pulmonary-Renal Syndrome

Systemic vasculitis	Anti-GBM disease (Goodpasture) ANCA associated Granulomatosis with polyangiitis (Wegener) Microscopic polyangiitis Churg-Strauss syndrome Drugs (penicillamine, hydralazine, propylthiouracil) Immune complex disease Lupus erythematosus Henoch-Schönlein purpura Mixed cryoglobulinemia Rheumatoid vasculitis
Infection	Severe bacterial pneumonia; postinfectious glomerulonephritis; Legionella; hantavirus; opportunistic infection in immunocompromised patients; infective endocarditis
Pulmonary edema and AKI	Volume overload; severe left ventricular failure
Multiorgan failure	Acute respiratory distress syndrome and AKI
Other	Paraquat poisoning; renal vein or IVC thrombosis with pulmonary emboli

## Causes of Rhabdomyolysis

Muscle injury, ischemia	Trauma, pressure necrosis, electric shock, burns, acute vascular disease
Myofiber exhaustion	Seizures, excessive exercise, heat exhaustion
Toxins	Alcohol, cocaine, heroin, amphetamines, ecstasy, phencyclidine, snakebite
Drugs	Statins, fibrates, zidovudine, neuroleptic malignant syndrome, azathioprine, theophylline, lithium, diuretics
Electrolyte disorders	Hypophosphatemia, hypokalemia, excess water shifts (hyperosmolarity)
Infections	Viral (Influenza, human immunodeficiency virus [HIV], Coxsackievirus, Epstein-Barr virus), bacterial (Legionella, Francisella, Streptococcus pneumoniae, Salmonella, Staphylococcus aureus)
Familial	McArdle disease, carnitine palmitoyl transferase deficiency, malignant hyperthermia
Other	Hypothyroidism, polymyositis, dermatomyositis



## Causes of Acute Kidney Injury in Patients with Cancer

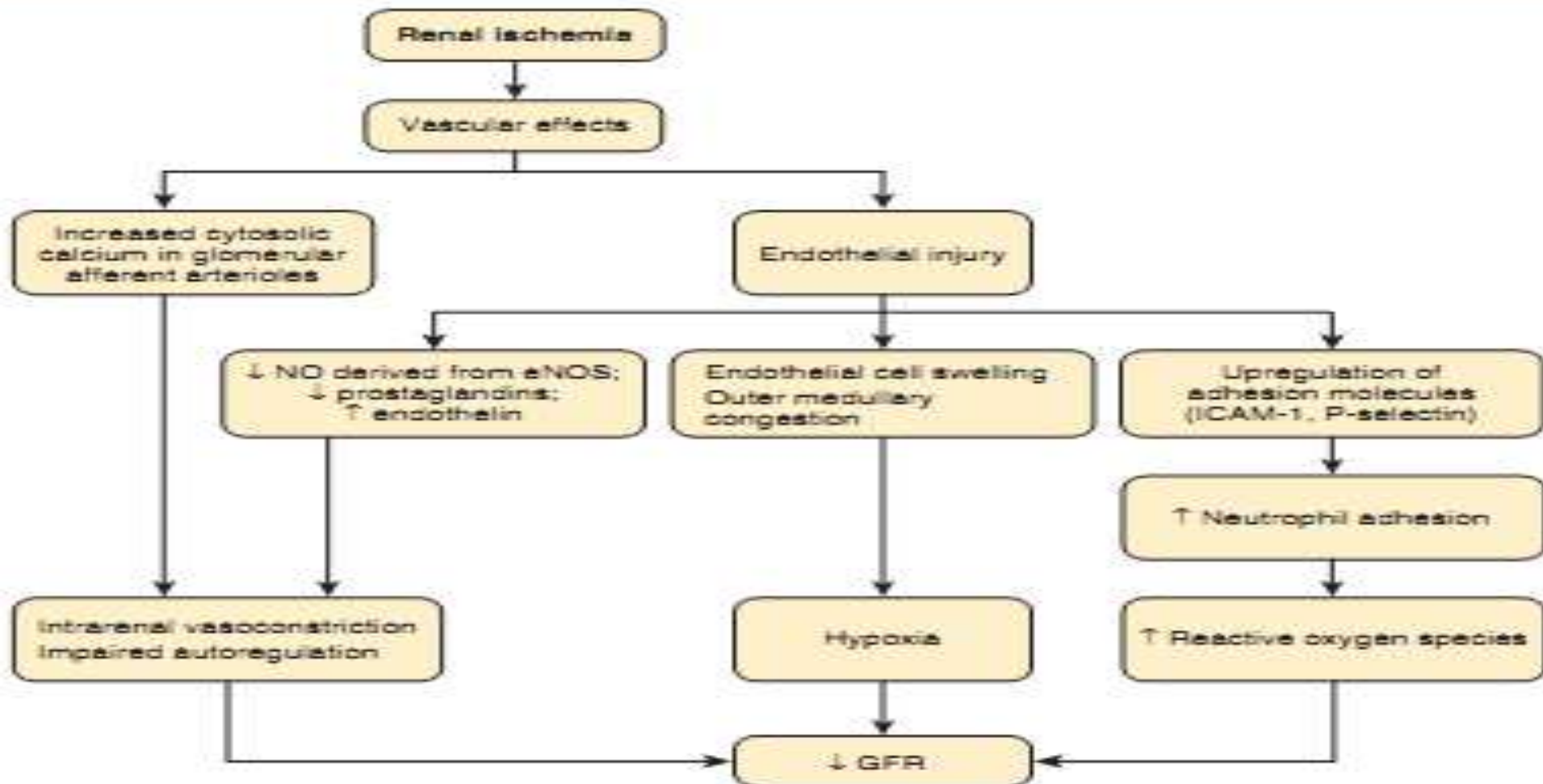
Pre-renal	Nausea and vomiting, hypercalcemia, cardiomyopathy secondary to chemotherapy
Vascular	Thrombotic microangiopathy (adenocarcinoma of stomach, pancreas, prostate; radiation nephropathy), renal vein thrombosis secondary to hypercoagulability, disseminated intravascular coagulation (acute promyelocytic leukemia)
Glomerular	Rapidly progressive glomerulonephritis
Acute tubular necrosis	Sepsis and antibiotic nephrotoxicity, hypercalcemia
Malignant infiltration	Lymphoma, acute lymphoblastic leukemia
Intraluminal obstruction	Tumor lysis syndrome, cast nephropathy
Post-renal obstruction	Transitional cell carcinoma of the ureters and bladder, extrinsic ureteral compression (tumor, nodes, retroperitoneal fibrosis)
Chemotherapeutic agents Tubular toxicity	Cisplatin, ifosfamide, plicamycin (mithramycin), 5-fluorouracil, thioguanine (6-thioguanine), cytarabine
Thrombotic microangiopathy	Mitomycin C, bleomycin, cisplatin, calcineurin inhibitors
Other mechanisms	Capillary leak syndrome (IL-2 therapy), acute interstitial nephritis (interferon- $\alpha$ ), intraluminal obstruction (methotrexate)

## Causes of Acute Kidney Injury and Liver Disease

Pre-renal uremia	Diuretic use, gastrointestinal loss, peritoneal aspiration, hypoalbuminemia
Hepatorenal syndrome	
Acute tubular necrosis	Hyperbilirubinemia, sepsis, toxic shock syndrome
Drugs	Acetaminophen (paracetamol), NSAIDs, tetracycline, rifampin, isoniazid, anesthetic agents, sulfonamides, allopurinol, methotrexate
Infections	Hepatitis C and cryoglobulinemia, hepatitis B and polyarteritis nodosa, leptospirosis, hantavirus, Epstein-Barr virus, gram-negative sepsis, spontaneous bacterial peritonitis
Other	Papillary necrosis and obstruction, inhalation of chlorinated hydrocarbons, mushroom poisoning ( <i>Amanita phalloides</i> )

# Pathophysiology

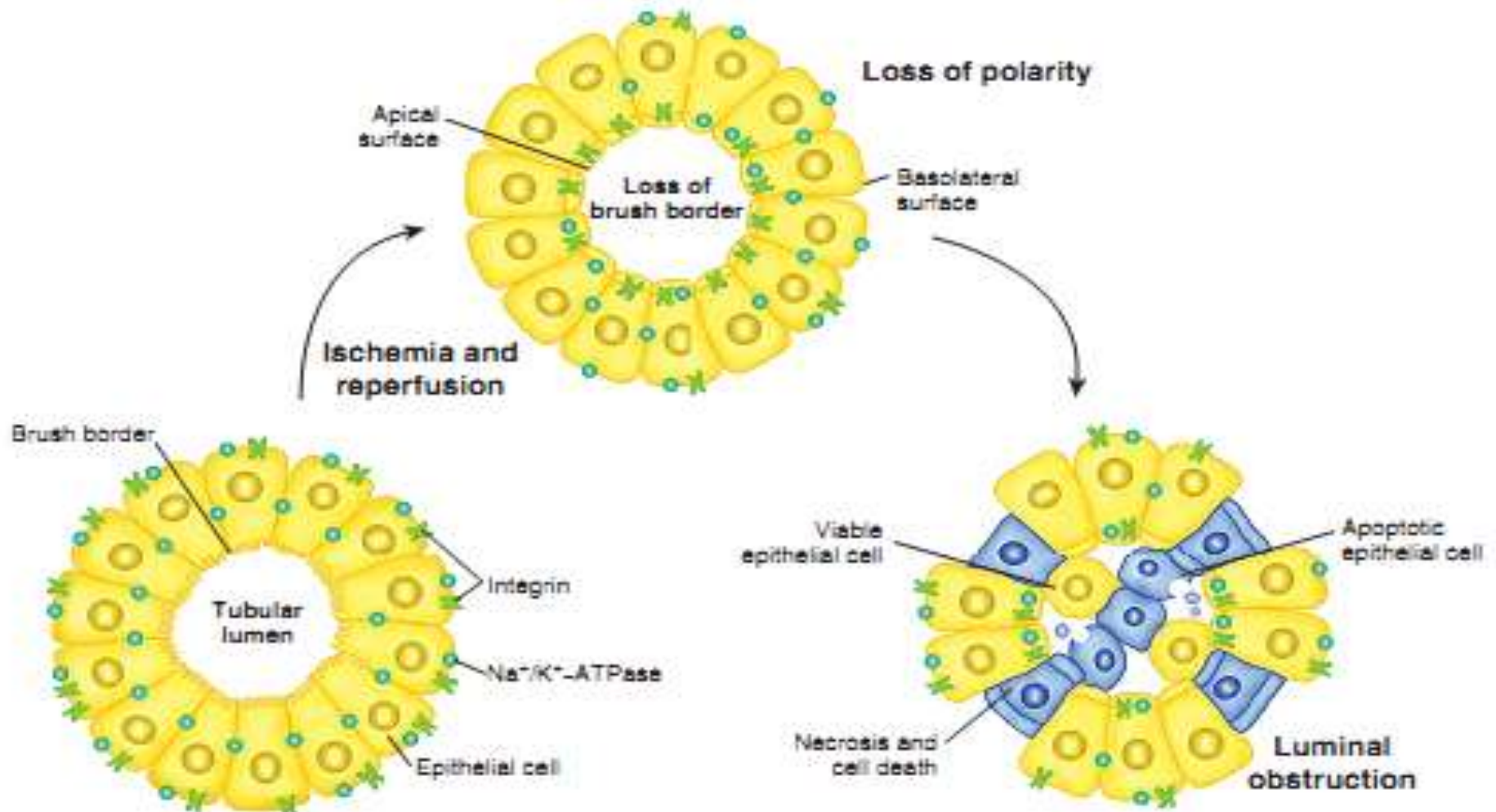
## Vascular Factors Contributing to the Development of Acute Tubular Necrosis





# Contd.,

## Tubular Factors in the Development of Acute Tubular Necrosis



# Sepsis and Acute Kidney Injury

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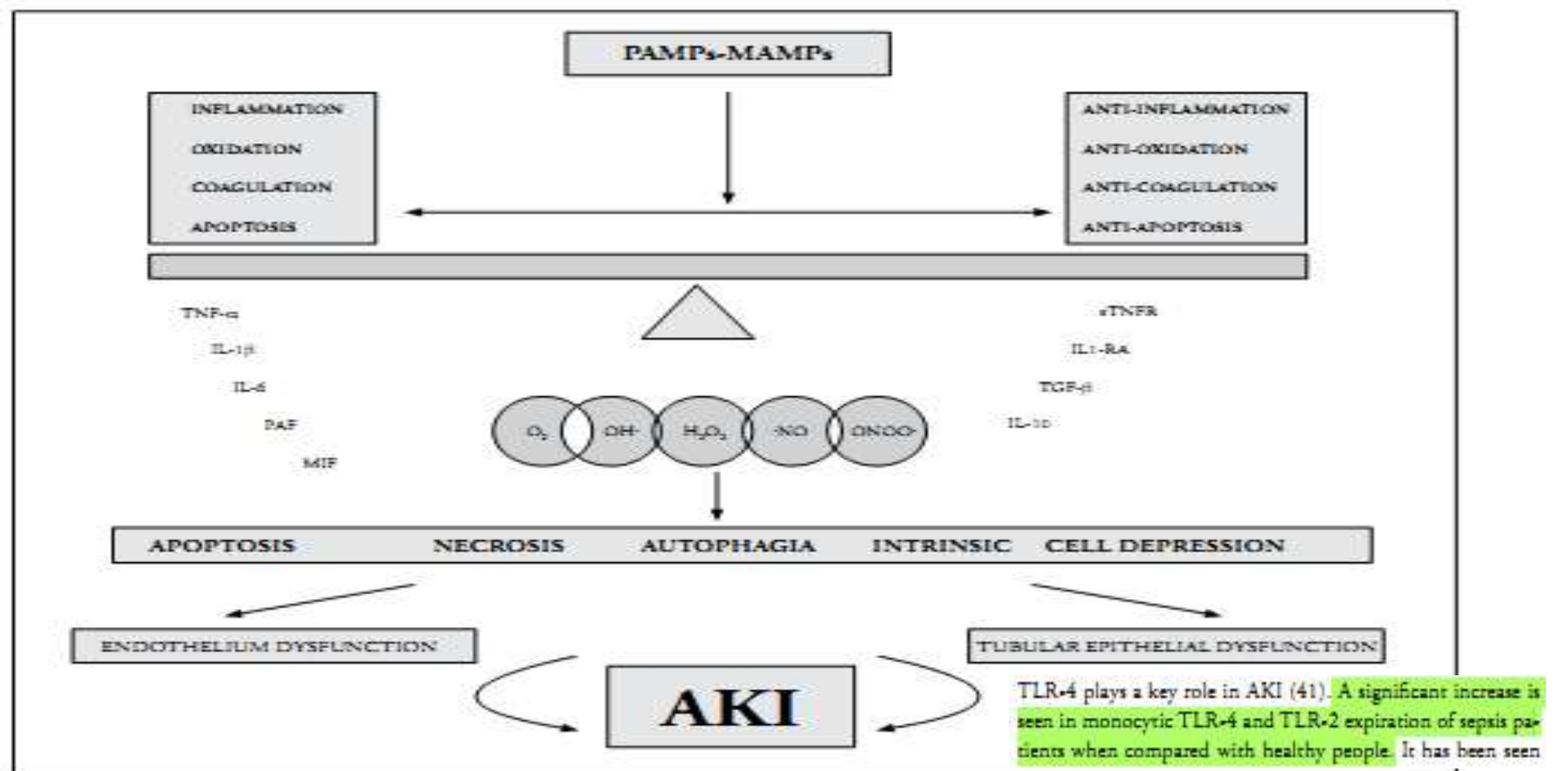
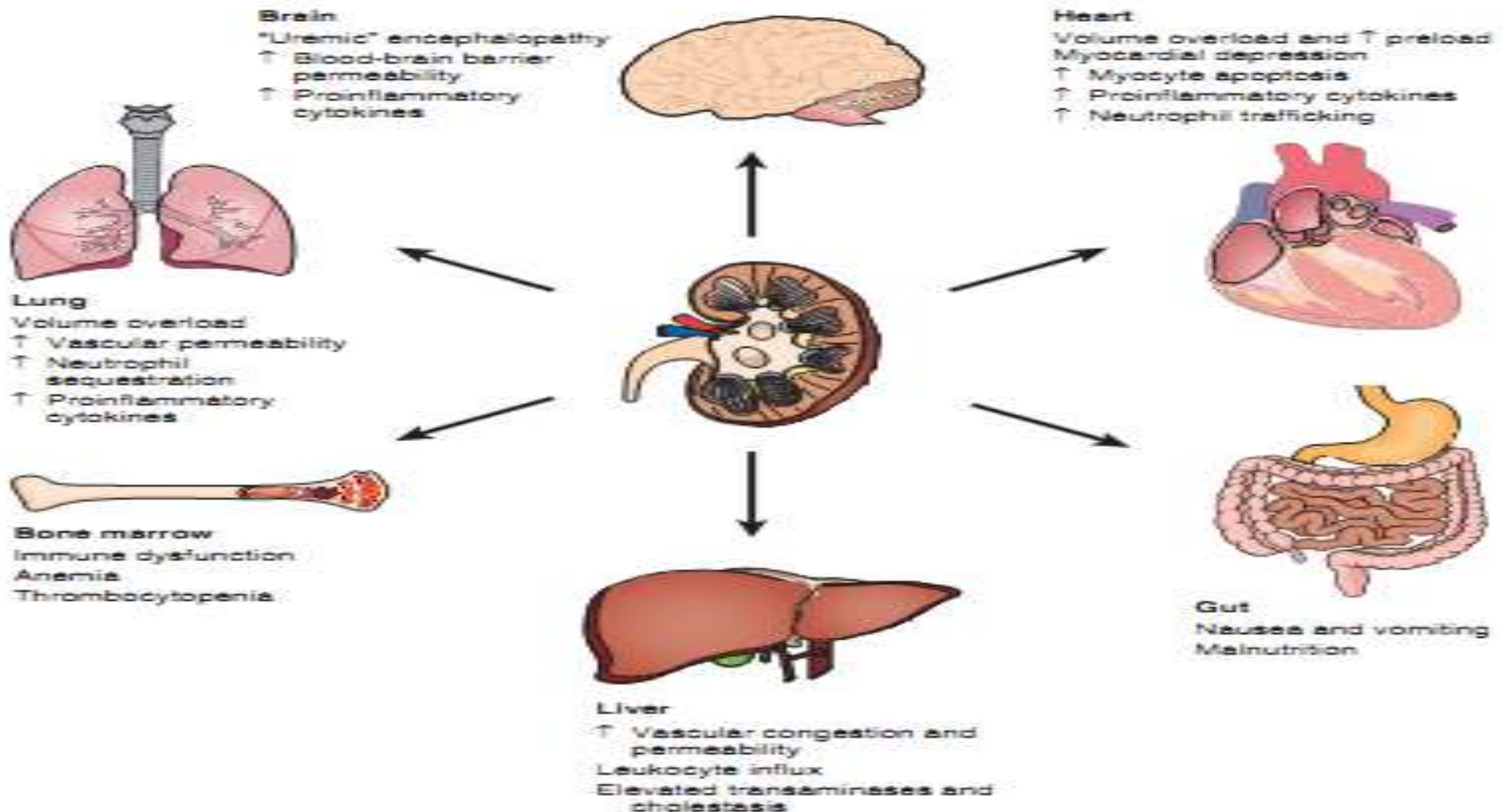


Figure 1. Key pathogenic pathways in sepsis and sepsis-associated-AKI pathophysiology

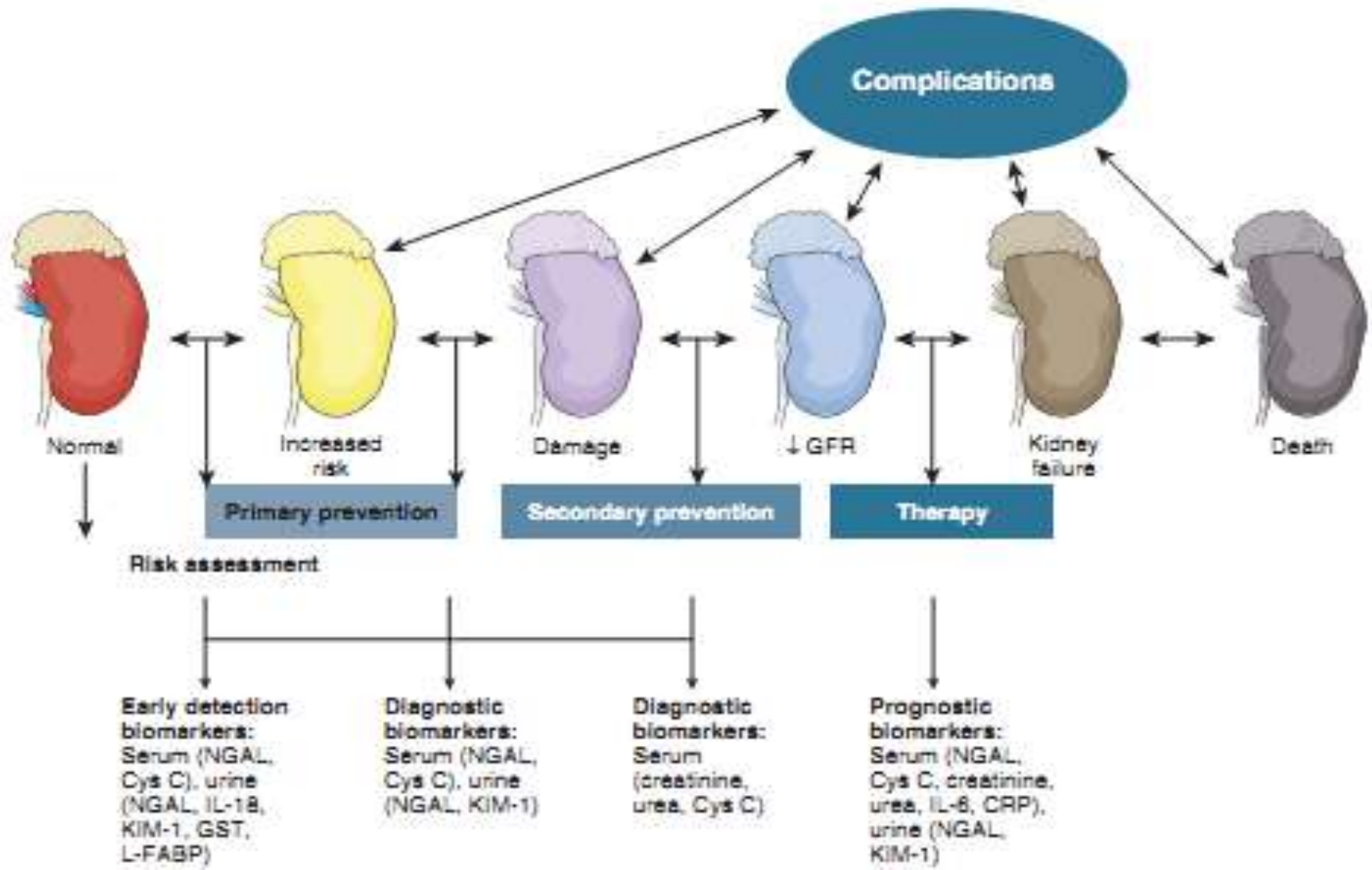
PAMPs: pathogen-associated molecular patterns; MAMPs: microbe-associated molecular patterns; TNF: tumour necrosis factor; IL: interleukin; PAF: procoagulating factor; MIF: migration inhibitory factor; HMGB: high-mobility group box; sTNFR: soluble tumour necrosis factor receptor; AKI: acute kidney injury

# Presentation

## Systemic Effects of Acute Kidney Injury



# Detection





# New markers

**Table 2: AKI biomarkers**

<b>Biomarker</b>	<b>Place of sample taken</b>	<b>Rising time in sepsis-associated AKI</b>
IGFBP-7	Urine	Very early
TIMP-2	Urine	Very early
NGAL	Plasma	Early
L-FABP	Urine	Early
Cystatin-C	Plasma	Moderate
KIM-1	Urine	Moderate
IL-8	Urine	Moderate

IGFBP-7: insulin-like growth factor binding protein; TIMP-2: tissue inhibitor of metalloproteinase-2; NGAL: neutrophil gelatinase-associated lipocalin; L-FABP: L-type fatty acid-binding protein; KIM-1: kidney injury molecule-1; AKI: acute kidney injury



# Contd.,

## Renal Angina



### Renal Angina equivalents

1. Oliguria
2. Small increases in SCr
3. Fluid overload



**In the presence of renal angina equivalents, significant research is essential!**

1. Biomarkers
2. Urinary microscopy
3. Urinalysis

Figure 3. Renal angina

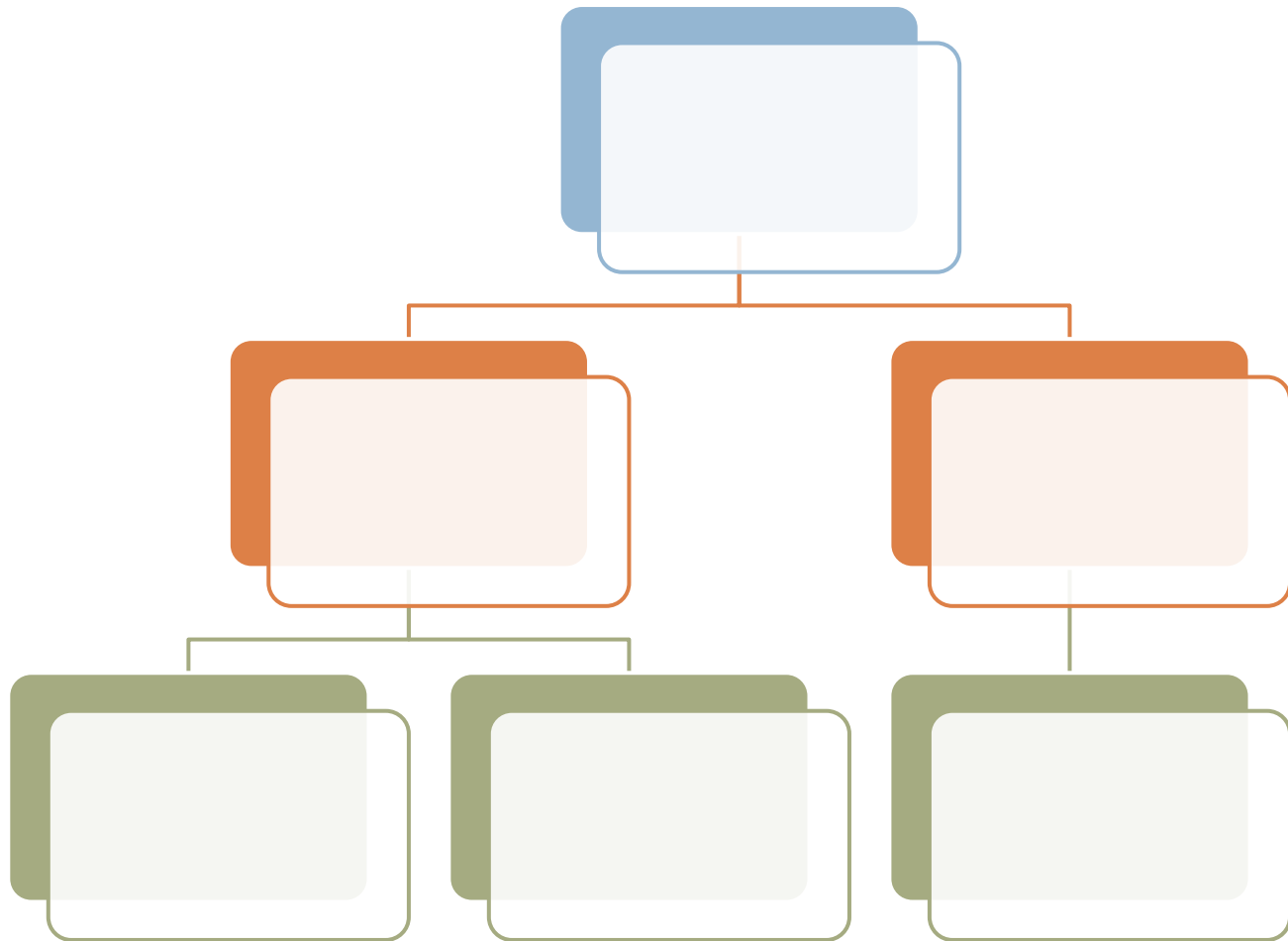
SCr: serum creatinine; AKI: acute kidney injury

# Management



AKI Stage				
High Risk	1	2	3	
Discontinue all nephrotoxic agents when possible				
Ensure volume status and perfusion pressure				
Consider functional hemodynamic monitoring				
Monitor Serum creatinine and urine output				
Avoid hyperglycemia				
Consider alternatives to radiocontrast procedures				
Non-invasive diagnostic workup				
Consider invasive diagnostic workup				
		Check for changes in drug dosing		
		Consider Renal Replacement Therapy		
		Consider ICU admission		
			Avoid subclavian catheters if possible	

# Contd.,



# LIFE is the most difficult EXAM.

Many people fail because they try to copy others -  
Not realising that everyone has a different question  
paper!

